III. REMARKS

Applicant acknowledges with thanks the courtesies extended by the examiner during the telephonic interviews of May 16, 2006 and May 18, 2006 during which the undersigned and the examiner discussed the structures of the inventive oligonucleotides of claim 1, the Uhlmann reference and the 35 USC 112 rejections.

Claims 1- 22 are in the case.

Claim Objections

Claims 1, 3-4 and 18 stand objected to for reciting incorrect structures of the claimed compounds. These claims have been amended to correct this error in recital.

Claim Rejections - 35 USC § 102

Claims 1-2, remain rejected and claims 5, 9-11 and 17 are rejected under 35 U.S.C. 102(b) as being anticipated by Uhlmann et al. for the reasons of record set forth Office Action mailed 11-17-03.

Applicants have modified the structure set forth in claim 1 to correspond with the specification which requires the existence of at least one phosphorothioate structure to permit non-specific binding to proteins. Thus at least one of the phosphate linkages is required to be modified to a phosphorothioate linkage. In addition, the claimed molecule must contain either a phosphoamidate or a PNA moiety, where the PNA moiety may be attached via a linker. [specification, page 5, last paragraph].

The structures of Uhlmann et al. do not anticipate the claimed chimeric oligonucleotides since the 3' end of the instantly claimed structures comprise an primary amine, and those compounds of Uhlmann et al. are terminated by a secondary amide, and furthermore because Uhlmann does not disclose the presence of phosphorothioate modifications of the phosphate

backbone in combination with a primary amine terminator.

Moreover, as stated in applicant's specification, since the compounds recited in Uhlmann et al. do not contain the specific structural modifications of the instant claims required for the instantly specified activity, absent evidence to the contrary, the compounds of Uhlmann et al. would not possess the functional characteristics of the compounds of the claimed invention.

For these reasons, applicants respectfully request reconsideration of this ground for rejection.

Claim Rejections - 35 U.S.C. s 112, first paragraph

As stated by the examiner claims 1-5, 7, 9-12, 14-15, and 17-18 stand rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for utilizing chimeric PNA oligonucleotides targeting the template region of telomerase RNA to inhibit telomerase activity *in vitro* or using phosphorothioate modified oligomers to non-specifically inhibit telomerase activity, does not reasonably provide enablement for using any generic non-phosphorothioate containing oligomeric compound of undefined sequence structure to inhibit telomerase activity.

Applicants have modified their claims to limit them to oligonucleotides targeting the template region of telomerase RNA to inhibit telomerase activity *in vitro* or using phosphorothioate modified oligomers to non-specifically inhibit telomerase activity. As recognized by the examiner, these oligos are enabled.

As stated by the examiner, applicants specification, at page 4 provides that the claimed invention encompasses the use of a genus of chimeric oligonucleotides, where it is necessary to replace at least a portion of the sugar phosphate backbone with either phosphorothioates for non-specific telomerase enzyme binding or to design oligomers to comprise N(2-amino ethyl)glycine targeting the template region of telomerase RNA to reduce telomerase activity in vitro.

Since it is recognized that there are known N(2-amino ethyl)glycine modified oligomers which could not be taken up by cell membranes, applicants overcome this problem in their invention by providing chimeric oligonucleotides that comprise both of the above aspects, namely a protein binding site, and a region that binds RNA, as set forth on page 5, paragraphs 3-6 of their specification.

As amended, the present claims claim structures which require the presence of phosphorothioate modifications and the presence of a phosphoroamidate or N(2-amino ethyl)glycine region targeting the template region of telomerase RNA, and the scope of the claims therefore does not read on oligonucleotides comprising a full sugar phosphate backbone.

With regard to chimeric oligonucleotides that comprise both of the above aspects, namely a protein binding site, and a region that binds RNA, as set forth on page 5, paragraphs 3-6, and specifically those exemplified as SEQ ID NO: 1-28, Applicants respectfully suggest that they have provided sufficient guidance and/or instruction for the skilled artisan to use the full scope of the claimed oligonucleotides in a method to inhibit telomerase activity without undue experimentation.

Applicants therefore respectfully request reconsideration of this ground for rejection.

Claim Rejection 35 USC § 112, first paragraph

Claims 8 and 12, and 14-15 stand rejected under 35 USC § 112, first paragraph.

The examiner rejects the Declaration under 37 CFR 1.132 filed 7-29-05 as insufficient to overcome the rejection of claims 8 and 12, and 14-15 based upon 35 USC § 112, first paragraph as set forth in the last Office action because the experimental data provided by Applicants was not commensurate in scope with the claimed invention.

However, applicant has now amended his claims such that the scope of the instant claims encompasses a plurality of antisense compounds that are limited to those antisense compounds

having the structure equivalent to those used to produce the results set forth in Applicant's Rule 1.132 Declaration.

As recognized by the examiner, the specification, is enabling for using chimeric oligonucleotides according to the present invention to inhibit telomerase activity *in vitro* comprising the administration of chimeric oligonucleotides, and provides guidance for inhibiting telomerase activity in human cancer cells transplanted into a nude mouse, but does not reasonably provide enablement for using chimeric oligonucleotides of undefined structure and/or target, *in vivo* for treating cancer in all non-human mammals.

Applicants have now defined the structure required of their molecules.

The examiner agrees that the Exhibit demonstrates enablement of the scope of the claimed invention that encompasses the inhibition of telomerase activity in human cancer cells transplanted into the flank region of a nude mouse, comprising the specific administration of:

Further, the disclosure of the ability of one particular sequence to function successfully to inhibit telomerase, specifically, SEQ ID NO: 28 and 23, while, as stated by the examiner, may not be sufficient to provide evidence of the ability of other compounds, the disclosure of compounds comprising a distinct sequence and modifications thereof that inhibit the expression of telomerase in a tumor cell *in vivo*, is evidence of the ability of closely related analogous compounds of defined sequence to function in the same manner.

Conclusion

Based on the foregoing remarks it is believed that the claim is in condition for allowance. However, should any issue(s) of a minor nature remain, the Examiner is respectfully requested to telephone the undersigned at telephone number (212) 808-0700 so that the issue(s) might be promptly resolved. If any extension of time for this response is required, Applicants request that this be considered a petition therefore. Please charge any insufficiency of fees, or credit any excess to Deposit Account No. 14-1263.

Respectfully submitted,
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By _____

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